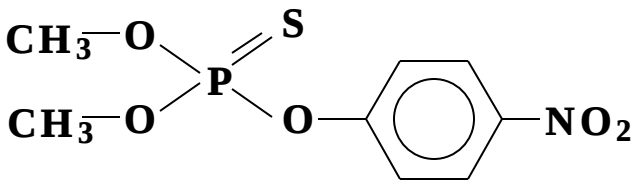
EVALUATION OF METHYL PARATHION AS A TOXIC AIR CONTAMINANT



Executive Summary

California Department of Pesticide Regulation

California Environmental Protection Agency
Sacramento, California

October 1999

TAC 99-02EX

Department of Pesticide Regulation

Paul E. Helliker
Director

For additional copies of this report please contact:

Department of Pesticide Regulation
Environmental Monitoring and Pest Management Branch
830 K Street
Sacramento, California 95814-3510

(916) 324-4100

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EXECUTIVE SUMMARY

What are the requirements of the Food and Agricultural Code for identifying pesticides as toxic air contaminants?

Signed into law in 1983 and 1984, respectively, Assembly Bills 1807 and 3219 establish the criteria necessary for the identification and control of TACs. AB 1807 mandates the Director of the Department of Pesticide Regulation (DPR) to determine which pesticides qualify as TACs in their pesticidal use (Food and Agricultural Code, § 14021 *et seq*.). AB 3219 sets specific timelines for the investigation and review of registered pesticides as possible TACs, requires public hearings in the TAC determination process, and enacts civil penalties for non-compliance of permit, use and mitigation conditions established by DPR. With respect to the evaluation and control of pesticides, this two-phase process separates risk assessment (identification of a pesticide as a TAC) from risk management (mitigation of exposure to pesticides that have been identified as TACs).

Current law requires DPR to prepare this three-part report—a health effects document that assesses the health effects and estimates levels of exposure for each candidate pesticide (FAC, § 14023). This report was reviewed by the Air Resources Board (ARB), the Office of Environmental Health Hazard Assessment (OEHHA), the Department of Health Services, the Scientific Review Panel (SRP), the pesticide registrants and the public. Following review and acceptance by the SRP, this report forms the basis for the Director's determination whether or not the pesticide is a TAC.

What is a toxic air contaminant (TAC)?

The Food and Agricultural Code (FAC) defines toxic air contaminants (TACs) as air pollutants that may cause or contribute to an increase in mortality or an increase in serious illness, or that may pose a present or potential hazard to human health (FAC, § 14023[d]). In addition, pesticides identified as federal hazardous air pollutants pursuant to section 7412 of Title 42 of the United States Code (FAC, § 14021), are also identified as TACs.

What is contained in this report?

The Evaluation of Methyl Parathion as a Toxic Air Contaminant is a three-part report. Part A—Environmental Fate was prepared by the Department of Pesticide Regulation's (DPR) Environmental Monitoring and Pest Management Branch. This section contains: (a) a review of the scientific literature concerning the environmental fate, and the physical and chemical characteristics of methyl parathion and its oxidative product, methyl paraoxon; (b) information regarding methyl parathion's applications, patterns of use, and formulations, relevant to California; (c) a review of the literature concerning airborne concentrations of methyl parathion and methyl paraoxon; and (d) the results of air monitoring studies conducted in California by the Air Resources Board's (ARB) staff. These studies were conducted to document airborne concentrations of methyl parathion and methyl paraoxon in California. Part B—Exposure Assessment was prepared by DPR's Worker Health and Safety Branch, and contains estimates of human exposure(s) to airborne methyl parathion and methyl paraoxon. Part C—Risk Assessment and Risk Characterization was prepared by DPR's Medical Toxicology Branch, reviews the health effects, and includes: (a) an assessment of the availability and the quality of data on health effects; and (b) the range of risk to humans resulting from the current or anticipated exposure to airborne methyl parathion and methyl paraoxon concentrations.

What is methyl parathion and how is it used?

Methyl parathion is an insecticide-acaricide sold in California for controlling insects, mites and other arthropods in cropland situations. It has the molecular formula $C_8H_{10}NO_5PS$, and a molecular weight of 263.21 AU. At room temperature methyl parathion is in the form of colorless crystals, which emit a faint garlic-like odor. Methyl parathion melts at 35-36 ºC, and has a boiling point of 119 ºC at 0.13 mBar. Methyl parathion has a vapor pressure of 2.3 mPa at 25 °C, a Henry's Law Constant of 10.3×10^{-8} atm•mole/m³, and its Specific Gravity (4/25 °C) is 1.265. Methyl parathion is sparingly soluble in water 55 mg/L at 25 ºC, is slightly soluble in petroleum distillates, and readily soluble in most organic solvents. In alkaline or acidic media, methyl parathion rapidly hydrolyzes.

Methyl Parathion is used in cropland situations to control insects and other invertebrate pests of more than thirty-five crops. It is also used to control pests in and around nurseries and nursery plantings, for public health control, regulatory pest control, and

landscape maintenance. Methyl parathion controls lepidopterous pests of alfalfa, almond, apricot, peach, and other stone fruits, small grains, peppers, sugarbeets and tomatoes. Methyl parathion is used extensively in rice cultivation for the control of the rice leafminer, and the tadpole shrimp. Methyl parathion is also used for the control of aphids, grasshoppers, leafminers, scale, spider mites, and other pests, and for the control of mosquitoes in irrigated pastures.

What is methyl paraoxon and how is it used?

Methyl paraoxon has the molecular formula $C_8H_{10}NO_5PO$ and a molecular weight of 247.14. There is no information regarding the physical or chemical properties of methyl paraoxon. Methyl paraoxon has never been registered for use as a pesticide, and has never been used as such.

What are the sources of methyl parathion and methyl paraoxon in the environment?

The sole source of methyl parathion in the environment derives from its use as a pesticide. The sole source of methyl paraoxon in the environment is from the oxidation of methyl parathion.

Five methyl parathion-containing products are currently (May 1999) registered for use in California. Formulations of methyl parathion include: four emulsifiable concentrates, and one microencapsulated product.

Use patterns of methyl parathion for 1990 through 1998 indicate that there is one seasonal peak in its use. This peak occurs in May, corresponding with two major cropland application scenarios. Methyl parathion is applied to rice in over a four to six week period in May and early-June. Commencing in May, methyl parathion is applied to stone fruits, over a slightly longer period of eight to twelve weeks, corresponding with its use in Rice. For most other cropland situations, methyl parathion applications are made on an as needed basis for the control of damaging insect populations. The fewest methyl parathion applications occur between November and February.

What is the fate of methyl parathion and methyl paraoxon in the environment?

In air, methyl parathion undergoes one of two reactions. The first involves hydrolytic degradation where methyl parathion is converted to two compounds of lesser toxicity, p-nitrophenol and dimethyl phosphorothioic acid. The second reaction is oxidative, and involves the phototransformation of methyl parathion to methyl paraoxon. This reaction is reported to occur rapidly in air when methyl parathion contacts hydroxyl radicals in the presence of ultraviolet light. Although the rate for this reaction is not known, once methyl paraoxon is produced, it is considered resistant to further atmospheric reactions.

The fate of methyl parathion in other environmental compartments is similar to its fate in air. In water, methyl parathion is converted to methyl paraoxon (reaction half-life = 44–96 hours) in the presence of hydroxy radicals and ultraviolet light. Methyl paraoxon further degrades via hydrolysis to dimethyl phosphoric acid and p-nitrophenol. In soils of high surface area or high organic matter, methyl parathion is generally found adsorbed to soil particles. In moist soils, where water content is below saturation and O_2 content is high, methyl parathion undergoes mineralization and is converted directly to dimethyl phosphorothioic acid and p-nitrophenol. *P*-Nitrophenol is then further hydrolyzed to p-aminophenol. However in flooded soils (soils in anaerobic conditions) methyl parathion is rapidly converted to methyl aminoparathion.

What are the reported concentrations of methyl parathion and methyl paraoxon in air?

In 1986, DPR requested the state Air Resources Board (ARB) to document the presence of methyl parathion in ambient air and in air associated with a specific pesticide application. The ARB subsequently requested the Environmental Toxicology Department, University of California at Davis, to perform the monitoring studies. Samples were collected in the communities of Maxwell and Williams in Colusa County, and Trowbridge and Robbins in Sutter County. Background samples were collected on the campus of the University of California, Davis in Yolo County.

The highest 24-hour average concentration of methyl parathion total residue (methyl parathion plus methyl paraoxon) for positive samples was 2.1 ppt measured at Maxwell. The mean 24-hour average methyl parathion concentration for positive samples in Colusa County was 0.8 ppt. In contrast, the mean 24-hour concentration of methyl parathion reported for

positive samples in Sutter County was less than 0.1 ppt. Background concentrations at Davis were below the Minimum Detection Limit (MDL) of 0.02 ppt.

Concentrations of methyl parathion in air reported in literature vary between 0.5 to 688.2 parts per trillion (ppt). Concentrations ranging from 101.8 to 688.2 ppt have been reported in 1- to 2-hour air samples, collected immediately following application at field boundaries. These levels decreased to 1.7 to 4.7 ppt over the six days following application. Air concentrations ranged from 0.5 to 188.5 ppt in 12- to 24-hour air samples collected at urban and rural sites (areas not associated with a particular application).

Air concentrations of methyl parathion were also measured during and after an application. Samplers were placed approximately 20 yards from a Sutter County rice field of approximately 80 acres. Eighty pounds of methyl parathion active ingredient (1lb AI/acre) were applied to this field. Samples were collected beginning at the onset of application, and then for three days. The highest average value, 47.6 ppt, was contained in the sample collected during and 1.5 hours after application. After 48 hours, methyl parathion concentrations were below 3 ppt.

Methyl Parathion use information was collected for townships (six miles by six miles square) in Colusa and Sutter counties. Eleven thousand six hundred pounds of methyl parathion were applied to townships immediately surrounding the sample collection station in Colusa County. Two thousand ten pounds of methyl parathion was applied to townships around the sampling station in Sutter County. No methyl parathion applications were reported near or around background samplers located in Yolo County over the course of sample collection.

The presence of methyl parathion in air is a dynamic process, and appears dependent on continual applications of the pesticide. Methyl parathion concentrations rise during application, level off for several hours and then begin to decline three to seven hours following application. From this point forward, methyl parathion concentrations begin to decline, and in the absence of further applications, will reach background levels within three to nine days. Since methyl paraoxon is an atmospheric breakdown produce its concentrations in air are expected to follow a similar scenario.

How will recent federal regulations affect the use of methyl parathion in California?

Recently, the United States Environmental Protection Agency, based on ongoing health concerns related to the use of methyl parathion, eliminated the continued use of methyl parathion on the following crops: apples, peaches, pears, grapes, nectarines, cherries, plums, carrots, certain peas, certain beans, and tomatoes. U.S.EPA has also eliminated uses on other fruits and vegetables (Federal Register: October 27, 1999, 64(207): 57877-57881).

Methyl parathion's use on rice (the use from which methyl parathion air concentrations were monitored for this document) has not been eliminated. Based on the continued use of methyl parathion on rice, the department feels that methyl parathion should be evaluated as a toxic air contaminant.

What are the expected exposures to airborne concentrations of methyl parathion and when do these exposures occur?

The exposure of residents of Colusa and Sutter County may be considered an extreme case scenario, since a substantial amount of the total State use of methyl parathion (20-30%) is typically applied to rice fields of northern California during a short period of time in May through mid June. The 1986 monitoring study in Sutter and Colusa Counties was used to estimate human exposure to methyl parathion in ambient air. Human exposure was calculated as an absorbed dosage based upon breathing rate and body weight for children and adult males and females. Children six years of age are the highest exposure subgroup because they have the highest inhalation rate to body weight ratio.

Exposure to airborne pesticide depends on the rate of inhalation and the rate of inhalation varies with activity. Total 24-hour (daily) inhalation rate for each subgroup was calculated from the inhalation rate of each subgroup for various representative activities during the day based upon activity surveys.

A single day or acute exposure is expressed as the absorbed daily dosage (ADD). For this purpose, the 95^{th} percentile of the measured airborne methyl parathion concentration was calculated for each location. Seasonal exposure is expressed as the seasonal average daily dosage (SADD). The average (arithmetic) airborne chemical level for each location over the entire monitoring period was used to calculate SADD. An annual estimate of exposure (the

annual average daily dosage, or AADD) was derived by assuming that air levels equivalent to the SADD could occur for nine months in a year.

Data from the Colusa and Sutter County study showed peak air levels in mid May, which corresponded to peak use periods. Estimated methyl parathion ADD ranged from 0.14 to 22 ng/kg/day. Methyl parathion SADD ranged from 0.05 to 6.2 ng/kg/day, and AADD ranged from 0.04 to 4.7 ng/kg/day. Methyl paraoxon exposures were approximately five fold lower than exposure to methyl parathion. Methyl paraoxon ADD ranged from 0.34 to 4.3 ng/kg/day, SADD from 0.17 to 1.3 ng/kg/day and AADD from 0.13 to 1.0 ng/kg/day. Children consistently had the highest estimated exposure per unit body weight followed by adult males. Exposures in Trowbridge and Robbins were typically more than ten fold lower than exposures calculated for Maxwell and Williams.

Human acute exposure or ADD to the application site air was also estimated, using two application site air monitoring studies. ADD ranged from 89 ng/kg/day for an adult female to 360 ng/kg/day for a child. No seasonal or chronic exposure to the application site air levels is expected since methyl parathion may be used only once, or the most, up to five times to a crop site during a season.

What are the potential acute, subchronic, and chronic non-carcinogenic health effects of methyl parathion?

The primary health effect of methyl parathion is its toxicity to the nervous system. One well-characterized mechanism for the neurotoxicity is the inhibition of cholinesterase (ChE). Cholinesterase is an enzyme that hydrolyzes acetylcholine (ACh), a neurotransmitter at nerve synapses. In addition to the inhibition of ChE in the blood that can be monitored in humans, toxicity studies in laboratory animals also revealed ChE inhibitions in the brain. In acute toxicity episodes, over abundance of ACh at effector sites, as a result of ChE inhibition, is manifested through muscarinic and nicotinic, as well as the central nervous system (CNS) symptoms. The symptoms and their severity vary, depending on the levels of exposure beyond a threshold. Peripheral muscarinic effects can include increased intestinal motility, bronchial constriction, increased bronchial secretions, incontinence, miosis, secretory gland stimulation, hypertension, and bradycardia. Peripheral nicotinic effects include muscle weakness, "twitching", "cramps", and general fasciculations. Stimulation of muscarinic and nicotinic receptors in the central nervous system can cause headache, restlessness, insomnia,

anxiety, slurred speech, tremors, ataxia, convulsions/seizures, depression of respiratory and circulatory centers, and coma. Death from lethal exposure is usually due to respiratory failure from a combination of central and peripheral effects (i.e., respiratory center depression, ventilation muscles weakness and paralysis, excessive tracheobronchial secretions, bronchoconstriction).

Effects other than the above signs of ChE inhibition were identified in laboratory animals. Exposures to methyl parathion resulted in neurobehavioral changes and nerve degenerations. Methyl parathion decreased the survival and body weight of rat pups in 2- and 3-generational reproductive toxicity studies and caused male and female reproductive toxicities. Pre-natal exposure to methyl parathion resulted in lower fetal body weight, increased resorption, reduced pup survival, and abnormalities and variations of in fetal ossification in rats and rabbits. Neurobehavioral changes were also observed as a result of *in utero* exposures. Methyl parathion did not show the organophosphorus-induced delayed neuropathy (OPIDN) in hens. Methyl parathion was found to suppress the immune system and caused hematological changes in rats. The existing limited data suggested an endocrine disruption potential for methyl parathion.

Of particular interest were the most sensitive toxicity endpoints, those effects that occurred at the lowest dose or exposure level. Threshold exposures based on these endpoints were used as references to assess the potential risk of exposures in humans. Although limited toxicity data in humans were available, more reliable data and more sensitive endpoints were identified in laboratory animals. They were plasma, red blood cell or RBC, and brain ChE inhibition, and neurological (nerve degeneration, functional neurobehavioral changes) and hematological (decreased RBC, hemoglobin, and hematocrit) effects. Separate NOELs (No-Observed-Effect Levels) were established for these endpoints and used to characterize the risk of the potential human exposures. NOEL is the lowest dose at which no effects are observed. The NOELs established based on data in laboratory animals for these effects ranged from 0.003 to 0.029 mg/kg/day for the acute (one to several days), seasonal (a season of pesticide use or exposure), and chronic (yearly) exposures.

Is there any potential cancer risk from exposure to methyl parathion?

The overall database showed that methyl parathion is genotoxic in laboratory studies and has the potential to cause changes in the cellular genetic material in humans. There is

limited evidence of increased tumor incidences in rodents after long-term exposures to methyl parathion. However, the overall oncogenicity (cancer-causing) weight of evidence was insufficient for a quantitative risk assessment. The risk of exposures to methyl parathion in humans is characterized based on the potential for non-oncogenic (or, non-cancer-causing) effects.

Does the concentration of methyl parathion in ambient air pose a potential health hazard for humans?

The combined exposure to methyl parathion and methyl paraoxon in the ambient air was estimated based on the 1986 monitoring studies conducted for rice applications in California. The risk was characterized in terms of a margin of exposure (MOE). The MOE is the ratio of the NOEL to the estimated human exposure. Based on the estimated exposures, the MOEs for the acute ambient air exposure were 4,800 - 19,000 based on the human NOEL and 390 - 1,600 based on the NOEL for sensitive endpoints in rats but not examined in humans. The MOEs for the ambient seasonal exposures were 16,000 - 65,000 based on the human NOEL, 1,000 - 4,200 based on the NOEL for sensitive endpoints in rats, and 150 - 630 based on plasma ChE inhibition. The MOEs for ambient chronic exposures were 1,300 - 5,400 based on the NOEL established in rats, and 670 - 2,700 based on RBC CHE inhibition in rats. For the exposures at the application site (17 and 20 yards from the rice field), the MOEs were 250 - 1,000 based on the human NOEL, and 20 - 80 (at 17 yards) based on the NOEL in rats. The lower value of the range of MOEs for each exposure scenario represents the MOE for a child and the higher value the MOE for a female adult.

For the ambient air exposure, the acute MOEs were 390 (for a child) - based on ChE inhibition (plasma, RBC, brain) as well as peripheral nerve degeneration in rats. The lowest seasonal MOEs were 150 based on plasma ChE inhibition in dogs and 1,000 based on RBC and brain ChE inhibition in rats. The lowest chronic MOEs were 670 based on RBC ChE inhibition in rats and 1,300 based on brain ChE inhibition, nerve degeneration, abnormal gait, hematological effects in rats.

For the exposure at the application sites, the MOEs for acute exposures (on a 24-hour basis) at 17 and 20 yards from a rice application field were as low as 20 based on ChE inhibition (plasma, RBC, brain) and peripheral nerve degeneration in rats.

The benchmark MOEs traditionally considered as adequate for the protection of human health is 100 based on a NOEL established in laboratory animals. This 100-fold MOE is based on current default assumptions that, on a dose per body weight basis, humans can be 10-fold more sensitive than the most sensitive laboratory animals (i.e., interspecies variation), and that there may be a 10-fold variation of sensitive among humans (i.e., intraspecies or inter-individual variation). There was an additional concern that methyl parathion may have the potential to cause developmental neurotoxicity. While a study specifically designed for this type of investigation is not available, USEPA required that an additional safety factor of 10 be applied for setting human exposure limits. This means that the benchmark MOE would be raised to 1,000.

The MOEs should be viewed in the context of the limitations and uncertainties in the assessment. These are presented in the risk appraisal section (Section 18.4) of the Part C, Human Health Assessment. This assessment does not include the risk from other pathways of exposure, such as oral ingestion of residues in foods. Nor does the assessment address the risk of any concomitant exposure to chemicals having the same mechanism of toxicity as methyl parathion (e.g., other organophosphates).

Do any of the degradation products of methyl parathion pose a potential health hazard?

Methyl parathion is oxidatively converted to the biologically active form methyl paraoxon through degradation in the environment and biotransformation in living organisms. Methyl paraoxon was shown to inhibit ChE activities. Only very limited toxicity data were available for methyl paraoxon. Based on these acute toxicity data in rats, a toxicity equivalence factor (TEF) of 10 for methyl paraoxon was established and used to account for the risk of methyl paraoxon concomitantly present with methyl parathion in the air. A TEF of 10 means methyl paraoxon could be as much as 10 times more toxic than methyl parathion for any toxicities identified in the database for methyl parathion. No toxicity data were available for any other environmental degradation products.